REMARKS

In the Office Action of March 25, 2003, the finality of the Office Action of June, 27, 2002 was withdrawn in light of Applicants' request for continued examination. In addition, the Office Action found a lack of unity of invention and, thus, required election of a single invention from Groups I – IV, as identified.

Applicants' request reconsideration of the finding of a lack of unity of invention in view of the following arguments. In the event that the arguments presented are not found to be persuasive, Applicants' provisionally elect, with traverse, the claims identified in Group I for examination.

Election / Restriction

The Office Action of March 25, 2003 separated the pending claims into four groups of inventions (Groups I-IV), which allegedly "are not so linked as to form a single general inventive concept under PCT Rule 13.1" because "under PCT Rule 13.2, they lack the same or corresponding special technical features." While the Examiner acknowledged that the inventions of groups I-IV "all relate to a detectable reagent comprising discrete particle dispersed in a carrier, diluent, excipient, adjuvant, wherein said particle comprises a detectable marker encased in at least two layers of carbon," she concluded that "the technical feature linking the inventions of groups I-IV does not constitute a special technical feature as defined by PCT rule 13.2, as it does not define a contribution over the prior art." In support of this assertion, the Examiner characterized the Burch *et al.* reference as teaching "Technegas (a plurality of discrete particles comprising a plurality of coating layers of carbon which completely enclose a minute crystal of 99m Tc metal) in an aqueous aerosol."

The methods and reagents in pending claims 31 – 79 relate to stable diagnostic and therapeutic colloids for the selective detection of fibrin in aqueous environments. Applicants agree with the Examiner's assertion that the pending claims share a technical feature in common in that they each involve "a detectable reagent comprising discrete particle dispersed in a carrier,

diluent, excipient, adjuvant, wherein said particle comprises a detectable marker encased in at least two layers of carbon." Applicants emphasize, however, that colloids of the present invention comprise carbonaceous particles dispersed in an aqueous medium. The combination of (i) selective binding to fibrin and (ii) stable association with an aqueous media exhibited by the diagnostic and therapeutic particles of the present invention provide "a technical relationship . . . involving one or more of the same or corresponding technical features . . . that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art." Patent Cooperation Treaty, Rule 13.2.

As conceded by the Examiner, pending claims 31 – 79 have a technical feature in common, namely use of diagnostic or therapeutic carbonaceous particles dispersed in an aqueous medium for the detection of fibrin. Applicant submits that searching for prior art relevant to all the claims of Groups I - IV does not present a significant burden because the pending claims are linked by such a specific and well defined technical feature. It is further submitted that the Examiner's conclusions regarding the scope of the contribution of the present invention to the prior art are better evaluated in the context of 35 U.S.C. §§ 102 and 103 statutory requirements.

In addition, the acknowledged technical features common to pending claims 31 – 79 do represent inventive contributions over the prior art because no prior art reference or combination of references teach diagnostic or therapeutic carbonaceous particles dispersed in an aqueous medium for detecting fibrin. Contrary to the Examiner's characterization, Burch *et al.* (1986) does **not** teach a plurality of discrete particles comprising carbon layers enclosing a crystal of 99m TC metal dispersed in an aqueous aerosol. Rather, Burch *et al.*'s teaching is limited to the formation of a diagnostic colloid comprising discrete carbonaceous particles dispersed in a gaseous argon continuous phase. Indeed, the particle formation process described in Burch *et al.* involves "evaporation **to dryness** of 140 MBq of sodium pertechnetate" in a graphite crucible by heating the crucible "to 2500° C in an atmosphere of pure argon." (*See*, Burch *et al.*, pg. 866, lines 18-24, emphasis added). Assuming a constant heat of vaporization of water of 44.016 kJ/mol as a function of temperature and a vapor pressure of water at 374 ° C of 1.65×10^5 Torr, the vapor pressure of water at the synthesis temperature employed in Burch *et al.*, 2500 ° C, is predicted to be approximately 1.16×10^5 Atm. (*see*, Exhibit A, a table from the Handbook of

Chemistry and Physics, 67th Ed., showing the vapor pressure of water as a function of temperature a table from Physical Chemistry by P.W. Atkins, showing heats of vaporization and an estimate of the vapor pressure of water at 2500°C). Any water in the system described by Burch *et al.* is in the gaseous state during particle formation. Therefore, it is not physically possible for water in the described particle generation system to be available as an aqueous medium (a liquid) for the dispersion of carbonaceous particles.

Further, there is no suggestion in Burch *et al.* to modify the diagnostic particles described therein to provide carbonaceous particles dispersed in aqueous media. Rather, Burch *et al.* teaches away from the use of particles in aqueous media. For example, Burch *et al.* note on page 866, lines 4 - 10, that the "many limitations" associated with aqueous aerosols of technetium prompted their investigation of non-aqueous diagnostic particles. Moreover, the reference reports the benefits of non-aqueous radioactive tracers exhibiting no "clearance from the lungs" and having long diagnostic half-lives. As Burch *et al.* does not disclose or even suggest the existence of carbonaceous, fibrin-binding particles dispersed in an aqueous medium, it cannot be relied upon as disclosing the technical feature linking the claims of Groups I-IV.

In view of the foregoing, it is submitted that the lack of unity of invention is improper. Accordingly, reconsideration and withdrawal of the lack of unity of invention is respectfully requested.

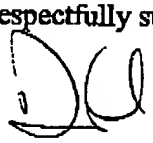
Conclusion

Based on the foregoing, this case is considered to be in condition for allowance and passage to issuance is respectfully requested.

This Amendment is accompanied by a Petition for Extension of Time. Please deduct the fee of $110.00 as required by 37 C.F.R. 1.17 from Deposit Account No. 07-1969. If this amount is incorrect, please deduct the appropriate fee for this submission from Deposit Account No. 07-1969.

If there are any outstanding issues related to patentability, the courtesy of a telephone interview is requested, and the Examiner is invited to call to arrange a mutually convenient time.

Respectfully submitted,



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DMF:lla:4/29/2003

VAPOR PRESSURE OF WATER ABOVE 100°C (continued)

Temp. °C	Pressure mm	Pressure Pounds per sq. in.	Temp. °F
208	13742.32	265.732	406.4
209	14022.76	271.156	408.2
210	14305.48	276.623	410.0
211	14595.04	282.222	411.8
212	14888.40	287.895	413.6
213	15184.80	293.626	415.4
214	15488.04	299.490	417.2
215	15792.80	305.380	419.0
216	16104.60	311.408	420.8
217	16420.56	317.523	422.6
218	16742.04	323.738	424.4
219	17067.32	330.028	426.2
220	17395.64	336.377	428.0
221	17731.56	342.872	429.8
222	18072.80	349.471	431.6
223	18417.84	356.143	433.4
224	18766.68	362.888	435.2
225	19123.12	369.781	437.0
226	19482.60	376.732	438.8
227	19848.92	383.815	440.6
228	20219.80	390.987	442.4
229	20596.76	398.276	444.2
230	20978.28	405.654	446.0
231	21365.12	413.134	447.8
232	21757.28	420.717	449.6
233	22154.00	428.388	451.4
234	22558.32	436.207	453.2
235	22967.96	444.125	455.0
236	23382.92	452.152	456.8
237	23802.44	460.264	458.6
238	24229.56	468.523	460.4
239	24661.24	476.871	462.2
240	25100.52	485.365	464.0
241	25543.60	493.933	465.8
242	25994.28	502.647	467.6
243	26448.52	511.450	469.4
244	26912.36	520.400	471.2
245	27381.28	529.467	473.0
246	27855.52	538.638	474.8
247	28335.84	547.926	476.6
248	28823.76	557.360	478.4
249	29317.00	566.898	480.2
250	29817.84	576.583	482.0
251	30324.00	586.370	483.8
252	30837.76	596.305	485.6
253	31356.84	606.342	487.4
254	31885.04	616.556	489.2
255	32417.80	626.859	491.0
256	32957.40	637.292	492.8
257	33505.36	647.888	494.6
258	34059.40	658.601	496.4
259	34618.76	669.417	498.2
260	35188.00	680.425	500.0
261	35761.80	691.520	501.8
262	36343.20	702.763	503.6
263	36932.20	714.152	505.4
264	37529.56	725.703	507.2
265	38133.00	737.372	509.0
266	38742.52	749.158	510.8
267	39361.92	761.135	512.6
268	39986.64	773.215	514.4
269	40619.72	785.457	516.2
270	41261.16	797.861	518.0
271	41910.20	810.411	519.8
272	42566.08	823.094	521.6
273	43229.56	835.923	523.4
274	43902.16	848.929	525.2
275	44580.84	862.057	527.0
276	45269.40	875.367	528.8
277	45964.04	888.799	530.6
278	46669.32	902.437	532.4
279	47382.20	916.222	534.2
280	48104.20	930.183	536.0
281	48833.80	944.291	537.8
282	49570.24	958.532	539.6
283	50316.56	972.963	541.4
284	51072.76	987.586	543.2
285	51838.08	1002.385	545.0
286	52611.76	1017.345	546.8
287	53395.32	1032.497	548.6
288	54187.24	1047.810	550.4
289	54989.04	1063.314	552.2
290	55799.20	1078.980	554.0
291	56618.40	1094.705	555.8
292	57448.40	1110.871	557.6
293	58284.40	1127.036	559.4
294	59131.60	1143.496	561.2
295	59984.40	1160.102	563.0
296	60860.80	1176.856	564.8
297	61742.40	1193.903	566.6
298	62624.00	1210.950	568.4
299	63528.40	1228.439	570.2
300	64432.80	1245.927	572.0
301	65352.40	1263.709	573.8
302	66279.60	1281.638	575.6
303	67214.40	1299.714	577.4
304	68156.80	1317.937	579.2
305	69114.40	1336.454	581.0
306	70072.00	1354.971	582.8
307	71052.40	1373.939	584.6
308	72048.00	1393.181	586.4
309	73028.40	1412.139	588.2
310	74024.00	1431.390	590.0
311	75042.40	1451.083	591.8
312	76076.00	1471.070	593.6
313	77117.20	1491.203	595.4
314	78166.00	1511.484	597.2
315	79230.00	1532.058	599.0
316	80294.00	1552.632	600.8
317	81373.20	1573.501	602.6
318	82467.60	1594.663	604.4
319	83569.60	1615.972	606.2
320	84686.80	1637.575	608.0
321	85819.20	1659.472	609.8
322	86959.20	1681.516	611.6
323	88114.40	1703.854	613.4
324	89277.20	1726.339	615.2
325	90447.60	1748.971	617.0
326	91633.20	1771.897	618.8
327	92826.40	1794.969	620.6
328	94042.40	1818.487	622.4
329	95273.60	1842.291	624.2
330	96512.40	1866.245	626.0
331	97758.80	1890.346	627.8
332	99020.40	1914.742	629.6
333	100297.20	1939.431	631.4
334	101581.60	1964.267	633.2
335	102881.20	1989.398	635.0
336	104196.00	2014.822	636.8
337	105526.00	2040.540	638.6
338	106871.20	2066.552	640.4
339	108224.00	2092.710	642.2
340	109592.00	2119.163	644.0
341	110967.60	2145.763	645.8
342	112358.40	2172.657	647.6
343	113749.20	2199.550	649.4
344	115178.00	2227.179	651.2
345	116614.40	2254.954	653.0
346	118073.60	2283.171	654.8
347	119532.80	2311.387	656.6
348	121014.80	2340.044	658.4
349	122504.40	2368.848	660.2
350	124001.60	2397.799	662.0
351	125521.60	2427.191	663.8
352	127049.20	2456.730	665.6
353	128599.60	2486.710	667.4
354	130157.60	2516.837	669.2
355	131750.80	2547.258	671.0
356	133326.80	2578.119	672.8
357	134945.60	2609.422	674.6
358	136579.60	2641.018	676.4
359	138228.80	2672.908	678.2
360	139893.20	2705.093	680.0
361	141572.80	2737.571	681.8
362	143275.20	2770.490	683.6
363	144992.80	2803.703	685.4
364	146733.20	2837.357	687.2
365	148519.20	2871.892	689.0
366	150320.40	2906.722	690.8
367	152129.20	2941.698	692.6
368	153960.80	2977.116	694.4
369	155815.20	3012.974	696.2
370	157692.40	3049.273	698.0
371	159584.80	3085.866	699.8
372	161507.60	3123.047	701.6
373	163468.40	3160.963	703.4
374	165467.20	3199.613	705.2

CRC Handbook of Chemistry and Physics

A Ready-Reference Book of Chemical and Physical Data

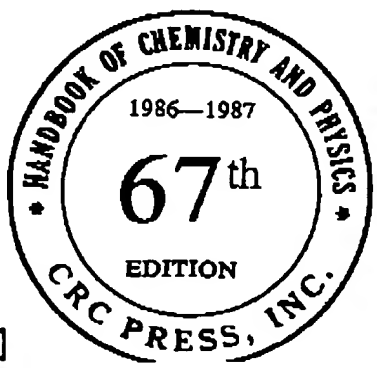

EXHIBIT A

Table 4.7. Enthalpies of fusion and vaporization at the transition temperature, $\Delta H_m^{\ominus}/kJ\ mol^{-1}$

	T_f/K	Fusion	T_b/K	Vaporization
Elements				
He	3.5	0.021	4.22	0.084
Ar	83.81	1.188	87.29	6.51
Xe	161	2.30	165	12.6
H_2	13.96	0.117	20.38	0.916
N_2	63.15	0.719	77.35	5.586
O_2	54.36	0.444	90.18	6.820
F_2	53.6	0.26	85.0	3.16
Cl_2	172.1	6.41	239.1	20.41
Br_2	265.9	10.57	332.4	29.45
I_2	386.8	15.52	458.4	41.80
Hg_2	234.3	2.292	629.7	59.30
Na	371.0	2.601	1156	98.01
Ag	1234	11.30	2436	250.6
Inorganic compounds				
H_2O	273.15	6.008	373.15	40.656 44.016 at ℉
Inorganic Compounds				
H_2S	187.6	2.377	212.8	18.67
NH_3	195.4	5.652	239.7	23.35
CO_2	217.0	8.33	194.6	25.23 (s) 30.00
CCl_4	250.3	2.47	349.9	26.74
CS_2	161.2	4.39	319.4	
H_2SO_4	283.5	2.56		
Organic compounds				
CH_4	90.68	0.941	111.7	8.18
C_2H_6	89.85	2.86	184.6	14.7
C_6H_6	278.6	10.59	353.2	30.8
CH_3OH	175.2	3.16	337.2	35.27 37.99 at ℉
C_2H_5OH	156	4.60	352	43.5

Data: AIP.

Library of Congress Cataloging in Publication Data
Atkins, P. W. (Peter William), 1940–
Physical chemistry.
Includes bibliographies and index.
1. Chemistry, Physical and theoretical. I. Title.
QD453.2.A88 1985 541.3 85–7048
ISBN 0–7167–1749–2

Estimate of the Vapor Pressure of Water at 2500° C

I. Assumptions and Boundary Conditions.

$\Delta H_{vap}(H_2O) = 44.016$ kJ mol^{-1}
$\Delta H_{vap}(H_2O)$ is constant as a function of temperature
$P_{vap}(H_2O, 374° C)) = 1.65 \times 10^5$ Torr = 217 Atm
$T_1 = 374° C$
$T_2 = 2500° C$

II. Estimate of $P_{vap}(H_2O)$ at 2500 ° C using the Clausius-Clapeyron Relationship.

$$\ln\left(\frac{P_{vap}^{T1}}{P_{vap}^{T2}}\right) = \left(\frac{\Delta H_{vap}}{R}\right) \times \left(\frac{1}{T_2} - \frac{1}{T_1}\right)$$

$$\ln\left(\frac{P_{vap}^{T1}}{P_{vap}^{T2}}\right) = \left(\frac{(44.016kJ)x\left(\frac{1000J}{1KJ}\right)}{8.3145JK^{-1}}\right) \times \left(\frac{1}{(2500+273)K} - \frac{1}{(374+273)K}\right)$$

$$\ln\left(\frac{P_{vap}^{T1}}{P_{vap}^{T2}}\right) = -6.28$$

$$P_{vap}^{T2} = \frac{P_{vap}^{T1}}{\exp(-6.28)} = \frac{217Atm}{0.00187} = 1.16 \times 10^5 Atm$$